

Amendments to the Specification:

Please replace the paragraph that bridges pages 15-16 of the specification with the following paragraph:

Computer implementations of these mathematical algorithms can be utilized for comparison of sequences to determine sequence identity. Such implementations include, but are not limited to: CLUSTAL in the PC/Gene program (available from Intelligenetics, Mountain View, California); the ALIGN program (Version 2.0) and GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Version 10 (available from Genetics Computer Group (GCG), 575 Science Drive, Madison, Wisconsin, USA). Alignments using these programs can be performed using the default parameters. The CLUSTAL program is well described by Higgins *et al.* (1988) *Gene* 73:237-244 (1988); Higgins *et al.* (1989) *CABIOS* 5:151-153; Corpet *et al.* (1988) *Nucleic Acids Res.* 16:10881-90; Huang *et al.* (1992) *CABIOS* 8:155-65; and Pearson *et al.* (1994) *Meth. Mol. Biol.* 24:307-331. The ALIGN program is based on the algorithm of Myers and Miller (1988) *supra*. A PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used with the ALIGN program when comparing amino acid sequences. The BLAST programs of Altschul *et al.* (1990) *J. Mol. Biol.* 215:403 are based on the algorithm of Karlin and Altschul (1990) *supra*. BLAST nucleotide searches can be performed with the BLASTN program, score = 100, wordlength = 12, to obtain nucleotide sequences homologous to a nucleotide sequence encoding a protein of the invention. BLAST protein searches can be performed with the BLASTX program, score = 50, wordlength = 3, to obtain amino acid sequences homologous to a protein or polypeptide of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST (in BLAST 2.0) can be utilized as described in Altschul *et al.* (1997) *Nucleic Acids Res.* 25:3389. Alternatively, PSI-BLAST (in BLAST 2.0) can be used to perform an iterated search that detects distant relationships between

molecules. See Altschul *et al.* (1997) *supra*. When utilizing BLAST, Gapped BLAST, PSI-BLAST, the default parameters of the respective programs (e.g., BLASTN for nucleotide sequences, BLASTX for proteins) can be used. See <http://www.ncbi.nlm.nih.gov>. Alignment may also be performed manually by inspection.

Please replace the paragraph that bridges pages 43-44 of the specification with the following paragraph:

Generation of a full-length tobacco MSH2 cDNA. The tobacco *MSH2* sequence was completed using a combination of 5' RACE, RT-PCR and inverse PCR (IPCR). Several upstream oligonucleotides were designed against amino acid motifs common to the *Arabidopsis thaliana* and *Saccharomyces cerevisiae* MSH2 proteins. These motifs included Y, MWLQP, MWLKQP (SEQ ID NO:34), E. The sequences of upstream oligonucleotides against these putatively conserved amino acid motifs were identical to the known *A. thaliana* cDNA sequence (Culligan and Hays (1997) *Plant Physiol.* 115:833-839). In each RT-PCR, an oligonucleotide designed to hybridize to the known tobacco *MSH2* sequence was used for the reverse transcription, and a nested oligonucleotide was used in conjunction with an upstream oligonucleotide for PCR. 5' RACE conditions followed the strategy of the Cap Finder 5' RACE kit (BRL). In short, purified reverse transcribed cDNA was 3' dC-tailed with terminal transferase (Promega) and dCTP. PCR of dC-tailed cDNA employed gene specific oligonucleotides and the G-anchor oligonucleotide (seq), using a cycling profile of 96°C for 13 sec., 55-60°C for 40 sec., 72° for 45 sec. IPCR was conducted on tobacco Nt-1 cell DNA digested with *Xba* I and recircularized by ligation, as reported elsewhere (Ochman *et al.* (1988) *Genetics* 149:641-650). Recircularized genomic DNA was amplified with two oligonucleotides; IPCR3 (5' AATGAAATGCAAGATTCTCC 3') (SEQ ID NO:27) and IPCR4 (5' GAAGCTTGCTCTGTTCTCC 3') (SEQ ID NO:28). PCR products were cloned by ligation into pGemT-Easy. Plasmid clones were sequenced on an ABI 310 automated sequencer, using the Big Dye Terminator kit (Perkin-Elmer, CT).

Please replace the paragraph on page 45 of the specification at lines 6-18 with the following paragraph:

Degenerate oligonucleotides were designed against two highly conserved MutS family signature amino acid motifs; TGPNM (SEQ ID NO:22) (5' ACNNGNCCNAAYATGGG 3') (SEQ ID NO:29) and FATHY (SEQ ID NO:23) (5' TGYAARTGNGTNCGR AA 3') (SEQ ID NO:30) (Reenan and Kolodner (1992) *Genetics* 132:963-973). Degenerate RT-PCR product subclones were screened by hybridization to an *A. thaliana* probe, comprising the corresponding region of the *A. thaliana MSH2* gene. Three candidate subclones were identified by southern analysis. The amplified sequence was highly homologous to the *A. thaliana MSH2*, and more similar to *MSH2s* than other *Msh* genes. A gene-specific oligonucleotide against the ATP binding site (5' CAGGCCCTAACATGGGTGG 3') (SEQ ID NO:31) was designed for 3' RACE. A 1.032 kb 3' RACE product was identified by hybridization to the previously identified sequences, which comprised the 3' end of the *MSH2* coding region, as well as the 3' UTR. Additional 5' *MSH2* cDNA sequences were obtained in a manner analogous to a chromosome walk utilizing degenerate RT-PCR and 5' RACE.

Please replace the paragraph that bridges pages 51-52 of the specification with the following paragraph:

The overexpression of a *MutS* homolog in an heterologous system can lead to a dominant mutator phenotype. To determine if the tobacco MSH2 could cause a mutator phenotype in *E. coli*, an (His)₆-tagged, IPTG-inducible plasmid clone (Qiagen, Valencia, CA) was constructed by cloning the nucleotides 1-797 of SEQ ID NO: 1, which encodes the N-terminal 265 amino acids of the tobacco MSH2 ((His)₆N) into pQE30 (Qiagen, Valencia, CA). The N-terminus of MutS has been shown to interact directly with DNA (Malkov *et al.* (1997) *J. Biol. Chem.* 272: 23811-23817) via a DYYT (amino acid positions 1-4 of SEQ ID NO:32) motif. This amino acid motif is present in all identified MSH2 proteins, including the tobacco homologue. Parallel fluctuation analysis was performed on 11 independent XL-1 blue (Stratagene, La Jolla CA) cultures containing either pBluescriptKS or (His)₆N plasmids. Mutation rates were determined by plating cells on LB plates containing 150 mg/L rifampicin and 100 mg/L ampicillin after 6 hrs. growth in 5 μ M IPTG. The total number of viable cells in each culture was estimated by counting ampicillin-resistant colonies from dilutions of the cell cultures.